Citation:

Cooper R, van Horn L, Liu K, et al. A randomized trial on the effect of decreased dietary sodium intake on blood pressure in adolescents. *J Hypertens.* 1984; 2: 361-366.

PubMed ID: 6530546

Study Design:

Randomized, controlled, crossover trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To assess the effect of moderate sodium reduction on blood pressure (BP) in healthy adolescents in a randomized controlled experiment.

Inclusion Criteria:

- Students at a Seventh-Day Adventist boarding school (Broadview Academy)
- Students consenting with signature of parent or guardian.

Exclusion Criteria:

Hypertension or chronic illness (although no students needed to be excluded for these reasons).

Description of Study Protocol:

Recruitment

Broadview Academy, a Seventh-Day Adventist boarding school for the high school years.

Design

Randomized, controlled, crossover trial.

Dietary Intake/Dietary Assessment Methodology

- Participants randomly assigned, after stratification for age and sex, to either the control or the experimental diet for Phase I (24 days), and then crossed over to the opposite diet for Phase II (24 days)
- A five-day vacation period (washout period) occurred between the two phases, during which time all students left the school and ate ad libitum

- Two serving lines were available at the cafeteria. Participants assigned to the experimental diet were served all meals from one line, while those on the control diet ate from the other line with the non-participating students.

Blinding

Students were not blinded, but data collectors were blinded to diet assignment.

Intervention

- All groups:
  - A four-week health education program was presented by the study nutritionist as part of the school curriculum before the initiation of the study
  - Program provided brief overview of the preventative approaches to the major cardiovascular diseases as well as background information pertaining to the significance of intended research
  - The institution serves a lacto-ovo-vegetarian cuisine, so no meat or fish products were used for either group. The institution has policies against the use of black pepper and other spices designated as irritants to the digestive system
  - No commercial centers were within walking distance of the school and there were no vending machines on campus
  - Participants were asked not to eat food sent from home
- Experimental diet:
  - Designed to approximate the control diet in nutrient content, except that sodium was reduced from an anticipated level of approximately 200mEq per 24 hours to a goal of 60mEq per 24 hours. The study nutritionist worked closely with the food service personnel to prepare special low-sodium menus controlled for sodium content in a way that would appeal to the teenage palate
  - Students were instructed not to add salt or other salt-containing condiments to their food during the experimental phase
  - Frozen or canned textured vegetable protein products typically served as entrée items were main sources of sodium excluded
  - Fresh fruits and vegetables, salads, unsalted nuts and specially prepared breads and dessert items were served during the experimental phase in lieu of high-sodium foods found in the regular menu cycle
  - Reduced sodium cheeses, peanut butter and salt-free margarine were obtained
  - Seasoning accomplished through the use of garlic, basil, thyme, oregano and mixtures of other herbs
  - Students requested not to consume foods obtained from other sources; between-meal snacks, such as fruit or juice, were provided by the cafeteria
- Control diet: “Normal” diet (lacto-ovo-vegetarian diet without meat or fish, and without the use of any black pepper or other spices designated as digestive irritants).

Statistical Analysis

No statistical plan or sample size calculation was provided.

Data Collection Summary:

Timing of Measurements

On days 1 and 24 of Phase I and on day 24 of Phase II, students were given appointments at

15-minute intervals between 6:00 a.m. and 12:30 p.m. for measurement of weight, height and BP.

Dependent Variables

- After the participant sat quietly without talking for 15 minutes, BP was measured with the right arm resting on a table at heart level. An initial pressure was measured with a standard mercury sphygmomanometer. A second BP was measured with a random-zero device after a 60-second pause. After another 60 second pause, a second measurement was made with the random-zero device. All blood pressures used for analysis were the mean of the two random-zero readings
- Radial pulse was counted for 30 seconds at two time points: Once before each random-zero device reading for BP
- Weight was measured on a balance scale with shoes off in indoor clothing
- Height was estimated by the device attached to the scales.

Independent Variables

- Family and medical history gathered via questionnaire at the time of consent
- Sodium intake was estimated by timed overnight urine samples. A randomly selected 10 participants from each group were asked to collect overnight specimens each week. Participants were instructed to void into the toilet before going to bed and record the time; on arising in the morning they were asked to void into the specimen container, record the time and return the specimen.
- Duplicate food samples were collected for 24-hour periods from a random sample of three participants per group per week. Identical portions were placed on a tray and condiments were added as used by the participant. The portion of food not eaten was removed from the duplicate tray after the meal and the residual, approximating the intake, was frozen and submitted to the laboratory for analysis.

Description of Actual Data Sample:

- *Initial N:* Of the 218 students living at the school, 132 initially volunteered and 124 actually began the study (60 boys and 64 girls). A severe winter storm prevented several students from returning from vacation for the baseline measurement on the first day of the study
- *Attrition (final N):* 113 completed the study.
    - During the first phase, five dropped out, (four unwilling to continue low-sodium diet, one left school)
    - During the second phase, three dropped out, (one was unwilling to continue low-sodium diet, two left school)
    - Three additional failed to appear for at least one examination.
- *Mean age:*
    - 16.3±1.3 years (Group I)
    - 16.2±1.2 years (Group II)
- *Other relevant demographics:* Despite randomized stratification, more boys than girls in Group I because of different dropout rates
- *Anthropometrics: G*roups similar
- *Location:* Rural setting approximately 40 miles west of Chicago, IL.

Summary of Results:

Blood Pressure During Sodium Reduction (Mean±SD)			
	Baseline	Phase I	Phase II
Group I (Control diet first, then experimental)			
SBP (mmHg)	108.0±10.1	103.5±10.0	102.1±9.8
DBP (mmHg)	59.6±10.3	62.0±10.8	62.7±13.9
Group II (Experimental diet first, then control)			
SBP (mmHg)	109.6±8.0	103.3±9.1	103.0±8.0
DBP (mmHg)	63.4±10.3	60.0±11.4	59.3±10.1

Change in Blood Pressure During Sodium Reduction (Experimental Minus Control; Mean±SD)				
Variable	Group I	Group II	Treatment Effect	Pooled T
SBP	-1.4±7.8	0.3±7.3	-0.6±0.7	-0.71
DBP	-3.4±10.7	0.7±11.3	-1.4±1.0	-1.31
Legend: Treatment effect=sum of Group I and Group II, divided by two; *P<0.05.				

Change in SBP During Sodium Reduction, Subgroup Analysis by BMI			
	Treatment effect (mean±SD; mmHg)		
Subgroup	Group I	Group II	Pooled T
BMI<23 kg/m2	-2.3±6.8	-1.1±7.7	1.92*
BMI>23 kg/m2	0.0±9.0	2.9±6.2	-1.27
Legend: *P<0.05			

Overnight Urinary Sodium, Potassium and Creatinine Excretion (Mean±SD)				
	N	Sodium (mEq)	Potassium (mEq)	Creatinine (mg)
Phase I				
Group I*	27	32.2±16.5	12.4±7.2	429.9±174.6
Group II†	21	9.1±6.9	9.4±5.1	350.6±147.2
Phase II				
Group I†	25	16.5±13.9	10.3±5.7	356.9±141.0
Group II*	23	29.6±24.5	9.2±7.5	313.6±197.6
Legend: *Control diet, †Experimental diet. N=number of separate overnight collections all values corrected for 8h.				

Other Key Findings

- A treatment effect (fall in BP) of 0.6mmHg was noted for SBP and 1.3mmHg for DBP
- Group I experienced a decrease in both SBP and DBP, group II experienced virtually no change in either
- Participants with BMI below the median (less than 23kg/m^2) experienced a significant 2mmHg decrease in SBP, while more obese participants had smaller, non-significant (NS) increases
- DBP did not change significantly in either BMI group
- A significant decrease in weight ($P<0.001$) and increase in heart rate ($P<0.05$) was also observed for participants with BMI less than 23kg/m^2.

Author Conclusion:

- Moderate sodium reduction does not appear to have an overall short-term effect on BP in normotensive adolescents
- Patients with BMI less than 23kg/m^2 experienced statistically significant reduction in SBP by 1.7mmHg, increase in pulse and decrease in weight. Possible that reduction in BP in this subgroup was subsequent to weight loss
- Control diet sodium content was actually 110mEq per 24 hours rather than 200mEq per 24 hours as previously thought, potentially minimizing the treatment effect by decreasing the difference in sodium intake between the two diets
- Restriction of sodium intake to 45mEq per 24 hours for periods of less than one month is insufficient to demonstrate effect on BP in a group of adolescents without special risk.

Reviewer Comments:

Limitations Noted by Reviewer

- *Limited reporting of demographics, health and other characteristics*
- *The subjects in this study may not truly represent the typical adolescent diet. The Seventh-Day Adventist institution only serves a lacto-ovo-vegetarian cuisine with no use of black pepper or spices and these students did not have access to foods outside the institution. This type of environment is not "free-living" since meals are provided by the school's cafeteria and the students have limited choice in what they eat. The diet provided by the school may not have the same amount of sodium found in the diet of the general population*
- *Although participants were stratified by gender upon randomization, the rate of dropout differed by gender, resulting in an imbalance between groups*
- *Subjects were not blinded to their treatment groups, so there is potential for them to change their eating habits even in the control group*
- *It is uncertain whether or not the reduction in sodium intake is sufficient to assess differences in BP between the two diets. It was originally thought that the control diet would contain 200mEq per 24 hours of sodium; however, sodium intake was estimated to be closer to approximately 110mEq per 24 hours*
- *There is no report of the plan for statistical analysis, so it is difficult to determine what methods were employed and if they were appropriate*
- *No sample size calculations were performed a priori so it is possible that the study was underpowered to detect differences in BP*
- *The calculation of treatment effect is not ideal. The most ideal scenario would be to find the*

change score from the end of the control diet compared to the end of the experimental diet within a single patient, and then determine the mean of the changes across the entire population with accompanying P-value from a paired T-test. The calculations presented here are unclear and may not accurately portray the differences in outcomes between the diets

- *The limited follow-up duration of 24 days may have been too short to see full effects of sodium intake on BP or weight*
- *Another factor that may have affected BP and weight would be exercise, but this was not accounted for*
- *The results were not adjusted for imbalances in gender (a potential confounding factor)*
- *The only statistically significant finding on BP was a 2.3mmHg reduction in SBP in the subgroup with BMI less than 23kg/m^2 but there was no discussion of the clinical relevance of this type of reduction.*

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Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	No
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	???
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	No

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	???
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		No
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	No
	8.2.	Were correct statistical tests used and assumptions of test not violated?	???
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
	8.6.	Was clinical significance as well as statistical significance reported?	No
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes